

What is Claimed is:

1. A method of eliciting a TLR8-mediated cellular response in a cell that expresses TLR8 comprising:
  - 5 selecting a compound identified as a TLR8 agonist; and
  - administering to the cell the compound in an amount that affects at least one TLR8-mediated cellular signaling pathway;
  - wherein the TLR8 agonist is a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged
  - 10 imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-
  - 15 imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.
2. The method of claim 1 wherein the cell is a monocyte, a macrophage, a dendritic cell, a B lymphocyte, a Natural Killer cell, a polymorphonuclear cell, or a cell
- 20 derived from any of the foregoing.
3. The method of claim 1 wherein the cellular response comprises NF- $\kappa$ B activation, production of at least one cytokine, production of at least one co-stimulatory marker, or any combination thereof.
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4. A method of treating an organism having a condition treatable by modulating a TLR8-mediated cellular response comprising:
  - selecting a compound identified as a TLR8 agonist; and
  - administering to the organism the compound in an amount effective to modulate
  - 30 a TLR8-mediated cellular signaling pathway;
  - wherein the TLR8 agonist is a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an

imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an  
oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a  
thiazolopyridine amine; an oxazolonaphthyridine amine; a thiazolonaphthyridine  
amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-  
5 imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine,  
naphthyridine amine, or tetrahydronaphthyridine amine.

5. The method of claim 4 wherein the organism is a mammal.

10 6. The method of claim 5 wherein the mammal is a human.

7. The method of claim 6 wherein the condition is a neoplastic disease.

8. The method of claim 6 wherein the condition is a T<sub>H</sub>2-mediated disease.

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9. The method of claim 8 wherein the condition is asthma, allergic rhinitis, or  
atopic dermatitis.

10 10. The method of claim 6 wherein the condition is a viral disease, a bacterial  
disease, a parasitic disease, a protozoal disease, or a prion-mediated disease.

11. The method of claim 4 wherein administering the IRM compound modulates  
NF- $\kappa$ B activity, the production of at least one cytokine, the production of at least one  
co-stimulatory marker, the production of an intercellular adhesion molecules, the  
25 production of a maturation marker, or any combination thereof.

12. A method of identifying a TLR8 agonist comprising:

a) exposing a TLR8-positive cell culture to a test compound and measuring  
a TLR8-mediated cellular response;

30 b) exposing a TLR8-negative cell culture to a test compound and  
measuring a TLR8-mediated cellular response; and

c) identifying the test compound as a TLR8 agonist if the cellular response in the TLR8-positive cell culture is greater than the cellular response of the TLR8-negative cell culture.

5        13.     The method of claim 12 wherein the TLR8-negative cell culture comprises cells that express a dominant negative variant of TLR8.

14.     The method of claim 12 wherein the TLR8-negative cell culture comprises antibodies raised against TLR8.

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15.     The method of claim 12 wherein the TLR8-positive cell culture comprises cells that overexpress TLR8.

15        16.     The method of claim 12 wherein the test compound is identified as a TLR8 agonist if the cellular response of the TLR8-positive cell culture is at least 20% greater than the cellular response of the TLR8-negative cell culture.

20        17.     The method of claim 12 wherein the test compound is identified as an TLR8 agonist if the cellular response of the TLR8-positive cell culture is at least 50% greater than the cellular response of the TLR8-negative cell culture.

18.     The method of claim 12 wherein the test compound is identified as a TLR8 agonist if the cellular response of the TLR8-positive cell culture is at least 80% greater than the cellular response of the TLR8-negative cell culture.

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19.     The method of claim 12 wherein the TLR8-mediated cellular response comprises NF- $\kappa$ B activation, the production of at least one cytokine, the production of at least one co-stimulatory marker or any combination thereof.

30        20.     A compound identified as a TLR8 agonist by the method of claim 12.

21.     A pharmaceutical composition comprising a TLR8 agonist in combination with a pharmaceutically acceptable carrier.

22. A method of identifying an TLR8 antagonist comprising:

a) exposing a first IRM-responsive cell culture to a TLR8 agonist and measuring a TLR8-mediated cellular response;

5 b) exposing a second IRM-responsive cell culture to a TLR8 agonist and a test compound, and measuring a TLR8-mediated cellular response; and

c) identifying the test compound as an TLR8 antagonist if the cellular response in the first cell culture is greater than the cellular response of the second cell culture.

10 23. The method of claim 22 wherein the TLR8 agonist is a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an  
15 oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazolonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.

20 24. A compound identified as a TLR8 antagonist by the method of claim 22.

25 25. A pharmaceutical composition comprising a TLR8 antagonist in combination with a pharmaceutically acceptable carrier.

26. The use of a dominant-negative variant of TLR8 to identify a compound that activates a TLR8-mediated cellular signaling pathway.

30 27. The use of an IRM compound as a positive control in an assay detecting activation of TLR8, wherein the IRM compound comprises a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an

oxazonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.

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28. A method of eliciting a TLR8-mediated cellular response in a cell that expresses TLR8 comprising:

selecting a compound identified as a TLR8 antagonist; and

administering to the cell the compound in an amount that affects at least one

10 TLR8-mediated cellular signaling pathway;

wherein the TLR8 antagonist is a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.

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29. A method of treating an organism having a condition treatable by modulating a TLR8-mediated cellular response comprising:

selecting a compound identified as a TLR8 antagonist; and

administering to the organism the compound in an amount effective to modulate  
25 a TLR8-mediated cellular signaling pathway;

wherein the TLR8 antagonist is a substituted imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; a 1,2-bridged imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazonaphthyridine amine; a thiazolonaphthyridine amine; a 6-, 7-, 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amine; or a 1*H*-

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imidazo dimer fused to pyridine amine, quinoline amine, tetrahydroquinoline amine, naphthyridine amine, or tetrahydronaphthyridine amine.